had an aphelion in the main asteroid belt and its perihelion was inside the orbit of the Earth, one-fifth of the way to the Sun.

On the night of 3 January 1970, another brilliant fireball lit up the sky over the central United States. As bright as the full Moon (magnitude −12), the meteor was photographed by the Prairie Fireball Network, and its orbit determined. On 10 January, the network team found a 10-kg meteorite lying on top of the snow in the middle of a road near Lost City, Oklahoma. Guided by a local resident who reported seeing glowing red lights and hearing a thud nearby, they found three other pieces, raising the total recovered mass to 17 kg, from an estimated pre-atmospheric mass of 75–200 kg. The Lost City meteorite is also classified as an ordinary H5 chondrite, and its orbit took it from the main belt to just inside the orbit of the Earth.

On 5 February 1977, another fireball of magnitude −12 was reported by an airline pilot flying over Saskatchewan, Canada. Members of the Meteorite Observation and Recovery Project recruited local youths to search for meteorites in the snow, and they found the first specimen near Innisfree, Alberta, on 17 February. Five more pieces were found in April after the snow had melted, and a farmer turned up another three. The total weight of all nine specimens came to 4.6 kg, from an estimated pre-atmospheric mass of 20–40 kg.

And that was it. No other meteorites had been recovered by fireball networks, until now. As Spurný *et al.*[1] report, the fourth meteorite was found on 14 July 2002, 6 km from the famous castle of Neuschwanstein (Fig. 1), after being photographed on 6 April 2002 by the successor to the original European Fireball Network. The fireball was of magnitude −17 and carved a luminous path 91 km long across the sky. Amazingly, it has been found to have an orbit identical to the Příbram meteorite, the first ever recovered (Fig. 3 on page 152). And yet, unlike Příbram (a fairly ordinary chondrite), Neuschwanstein is classified as an 'EL6 enstatite chondrite': it differs significantly from the other three in that it is more reduced (with less FeO in its silicates), it has lower ratios of Mg/Si and (Ca, Al, Ti)/Si, and it has a coarser granularity with little or no evidence of chondrules. Furthermore, Neuschwanstein has a cosmic-ray exposure age — a measure of the length of time that the body has been travelling through space — of 48 million years, compared with 12 million years for Příbram. So it seems that the meteor stream in which these objects were flowing is more heterogeneous than is usually assumed.

Looking skyward, knowing where these rocks came from, we may begin to understand something of the early history of our Solar System. Zdenek Ceplecha, now retired, must be delighted to see this new success of his fireball network. ■

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Mathematics

Conjuring with conjectures

Ian Stewart

The Clay Mathematics Institute is offering a million dollars for a solution to the Poincaré conjecture, and Grisha Perelman may have found one. What is the conjecture, and why does it matter?

In 1904, Henri Poincaré was making fundamental advances in topology — the multi-dimensional study of mathematical properties such as 'knotted' or 'connected', which are unchanged by continuous deformations. Buried in his work was an unjustified assumption about three-dimensional spaces. When he noticed it, and failed to find a proof, the assumption became first a question, and then a conjecture. Unsolved almost a century later, the Poincaré conjecture joined other problems (such as the Riemann hypothesis and Yang–Mills theory) on a list of 'Millennium Prize Problems' for whose solutions a substantial cash prize is offered[1]. Grisha Perelman of the Steklov Institute of Mathematics in St Petersburg, Russia, may now have found the answer[2,3].

The Poincaré conjecture can be understood by analogy with the case in two dimensions. A two-dimensional space, or surface, is like a bubble made from an infinitely thin film of soap. If the bubble is round, the surface is a sphere, but many other shapes are possible. A torus, for instance, is shaped like an American doughnut; a two-holed torus is like two doughnuts joined together, and so on.

The early topologists proved that any surface is topologically equivalent to a torus with a finite number of holes. A lumpy potato is the same as a sphere, a coffee-cup is the same as a torus, and a teapot is the same as a two-holed torus[4]. Poincaré sought a comparable understanding of three-dimensional spaces. The simplest is the three-sphere, analogous to a sphere but having three dimensions instead of two. This is almost the same as a solid ball, but only if you pretend that the entire outer surface of the ball is a single point.

The key problem is to decide whether a given surface — a lumpy potato, say — is equivalent to a sphere, or to something more exotic. Poincaré's predecessors had solved that problem in two dimensions, by working out how closed loops in the surface behave when they are moved. Any loop on a sphere can be continuously deformed, or shrunk, to a point. But on a torus, or a more complicated surface, many loops cannot be shrunk (Fig. 1a). Better still, if every loop can be shrunk then the surface must be a sphere. So the 'shrinkability' of loops provides a definitive test for spherical topology.

What about three dimensions? It is easy to prove that every loop in a three-sphere can be shrunk, but Poincaré tacitly assumed the converse: if every loop can be shrunk, then the space is topologically a three-sphere. Only later did it dawn on him that this statement — now called the Poincaré conjecture — was not obvious, and perhaps might not even be true.

Throughout the twentieth century, the conjecture remained as mysterious as ever. Analogous statements in all numbers of dimensions from four upwards had been proved true, but Poincaré's original three-dimensional problem still held out. The Poincaré conjecture had become a serious obstacle to any understanding of three-dimensional topology. Because topology is fundamental to many branches of mathematics, and to several areas of mathematical physics, this missing piece of the mathematical tool kit had become a serious embarrassment. How can we hope to understand the shape of our own Universe, for instance, when we don't even know the range of possibilities? And what about the even harder topological problems arising in quantum field theory (for example, in relation to string theory, where space-time has extra dimensions that curl up in some topological manner)?

Around 1983, William Thurston had devised an entirely new approach to the Poincaré conjecture, by relating it to classical geometry. Starting, again, in two dimensions, Thurston wondered why there are lots of shapes for a potato, but only one round sphere. What makes that shape special? It has constant (positive) curvature: every bit of a round sphere is bent the same amount as any other. Similarly, there is a 'canonical' geometry for a torus, and in this case the curvature is zero. The usual torus does not look flat, but a rectangle with opposite edges

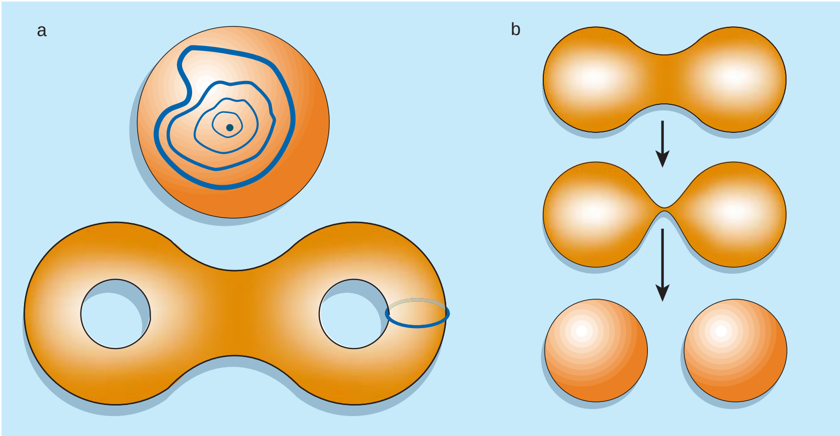


Figure 1 **Testing topology.** a, **On the surface of a sphere, every loop can be deformed to a single point. But on any other surface, such as the two-holed torus shown here, some loops cannot be deformed to a point. Topologically, these are two-dimensional objects, but in three dimensions the 'shrinkability' of loops becomes the basis of Poincaré's conjecture.** b, **Perelman's solution[2,3] to the Poincaré conjecture starts with 'Ricci flow': to achieve constant curvature of its surface, an object such as this dumbbell-shaped bubble splits into two round ones.**

identified is flat, and topologically that is a torus. Finally, tori with two or more holes can be realized as surfaces of constant negative curvature.

Thurston suggested that something similar should happen in three dimensions. He proved that exactly eight different 'geometries' can occur. It turned out to be too much to expect every three-dimensional space to have a single canonical geometry, but Thurston's 'geometrization conjecture' asserted the next best thing: every three-dimensional space can be cut up, in a systematic way, so that each piece has precisely one of those eight geometries. This new conjecture was much more ambitious than Poincaré's: it aimed at understanding all three-dimensional spaces, not just the three-sphere. In particular, the Poincaré conjecture was an easy consequence of the geometrization conjecture: the condition on loops meant that only one piece would be needed, and the associated geometry must be that of the three-sphere.

Perelman's work[2,3] is a new approach to the geometrization conjecture. If it pans out, it will constitute a huge leap forward in three-dimensional topology and mathematical physics. It is based on the Ricci flow, an idea of Richard Hamilton's[5]: if a soap bubble is deformed away from its normal round shape, surface tension will pull it back to a perfect sphere. The Ricci flow is an analogous way to deform any surface so that its curvature 'tries' to become constant. Along the way, though, it may have to split into separate pieces; for example, a dumbbell-shaped bubble must break up into two round ones (Fig. 1b).

Hamilton defined the Ricci flow in three dimensions, and developed a programme to prove that when a three-dimensional 'bubble' follows the flow, the pieces it breaks into are essentially those predicted by the geometrization conjecture. Perelman's papers do not carry out the entire Hamilton programme, but it looks as though they might establish enough of it to prove the geometrization conjecture. That in turn will prove the Poincaré conjecture.

If everything hangs together, a 99-year search is at an end. If not, Perelman's papers will still shed a huge amount of light on the Ricci flow, which is important in quantum field theory and pure mathematics, and may well pave the way to an eventual proof of the two conjectures. Either way, the spin-off is

Molecular physiology

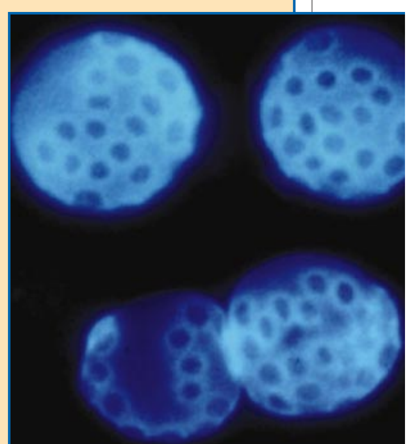
Tuned for longer life

Sometime early in the sixteenth century, 40-year-old Luigi Cornaro decided to cut his food intake dramatically for health reasons — he then lived on to the age of 102, writing treatises on the merits of his abstemious lifestyle. Five centuries later it is not clear whether severely limiting food consumption can, in general, extend human life, although calorie restriction does indeed extend the lifespan of commonly studied organisms such as yeast, nematode worms and mice. The latest turn of events is described by David A. Sinclair and colleagues elsewhere in this issue (R. M. Anderson *et al. Nature* **423,** 181–185; 2003). In studies of the yeast *Saccharomyces cerevisiae*, the researchers have pinpointed an enzyme, Pnc1, that seems to be a key link between environmental stress, metabolic energy and lifespan.

Sinclair and colleagues explore the control of an intriguing protein named Sir2 (silent information regulator 2), which has been shown to extend the lifespan of various laboratory organisms. Sir2 is a histone deacetylase, found in cell nuclei, where it is thought to turn genes on and off by influencing the packing of chromosomal DNA. Sir2 action requires the ubiquitous energy cofactor NAD^+, generating nicotinamide in the reaction, and nicotinamide also turns out to be a potent inhibitor of Sir2. But how exactly does metabolic energy affect Sir2 activity and lifespan?

The involvement of nicotinamide led Sinclair and co-workers to Pnc1, an enzyme that breaks nicotinamide down to nicotinic acid. They find that increasing the levels of Pnc1 in yeast leads to a dramatic lengthening of lifespan, as nicotinamide depletion results in Sir2 activation (yeast lifespan is usually measured by the number of buds, or daughters, produced by a given cell, individual bud scars showing up as darker circles on the blue-stained yeast cells shown here). Various types of stress are known to extend yeast life, including glucose restriction, high temperatures and elevated salt concentrations, and Pnc1 levels are raised in all of these circumstances. This suggests that Pnc1 is a key regulator of Sir2, and is responsible for tuning a yeast's lifespan and reproductive capacity to the quality of its environment.

Whether these ideas apply to multicellular organisms will have to be tested in worms and mice. On the one hand, one might imagine that mechanisms designed to protect single yeast cells from the vicissitudes of their environment would not be needed in more complex organisms, which possess homeostatic systems designed to protect and nourish individual cells.



JAMES CLAUS

On the other, lifespan is likely to be controlled by evolutionarily ancient mechanisms. So understanding Sir2 regulation in multicellular organisms, and identifying the genes that are controlled by Sir2 and its relatives, should prove generally rewarding. **Richard Turner**

likely to make profound changes to how we think about topology, space-time and quantum field theory. ■

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Prion diseases

Cannibals and garbage piles

Adriano Aguzzi and Mathias Heikenwalder

There's a lot of disagreement among prion scientists, as a recent conference made very clear. Even the revered 'prion hypothesis' came under attack.

After more than 280,000 mad cows and two Nobel prizes for research on transmissible spongiform encephalopathies, we must know all there is to know about these 'prion' diseases. Or do we? This question was asked at a recent symposium*, which looked at topics such as the cell biology of the normal prion protein and of its misshapen, disease-associated form; how the brain becomes damaged; and diagnosis and treatment. It was clear that, in all of these areas and more, there's still a long way to go.

Prion scientists have a reputation for being a contentious bunch — a fact that was amply confirmed on this occasion. Diametrically divergent opinions emerged on central questions such as the physiological function of the normal prion protein (PrP^C) and the role of its aberrant form (PrP^{Sc}) in disease.

Even the prion hypothesis, which nowadays is often regarded as dogma, was challenged. This hypothesis states that PrP^{Sc} is the infectious agent in transmissible spongiform encephalopathies (TSEs), and that it replicates by imparting its misshapen conformation onto PrP^C. In a spirited lecture, however, new Nobel laureate Kurt Wüthrich (ETH, Zurich) pointed out the continued failures to create infectivity *in vitro* by modifying bacterially expressed prion protein — a crucial prediction of the prion hypothesis. Another important experiment involves abolishing the structure (and infectivity) of the disease-associated prion protein with specific salts, and then attempting to restore infectivity by reinstating the original structure. This, too, has so far failed. Wüthrich referred to PrP^{Sc} as simply a build-up of "garbage", and submitted that we must understand the function of the normal prion protein before we can understand prion diseases.

The TSEs are characterized by the death of nerve cells, and another point of controversy concerned the mechanisms by which this occurs. A strong case was presented that the accumulation of PrP^{Sc} within the cytosol of neurons is to blame (S. Lindquist, Whitehead Inst., Cambridge, Massachusetts)[1,2]. PrP^C is usually located in the plasma membrane, and travels there by way of a network of internal membranes, the endoplasmic reticulum (ER). Lindquist proposed that a certain proportion of PrP^C never reaches the plasma membrane, but instead re-enters the cytosol by 'retrotranslocation' from the ER — a standard means by which other misfolded proteins are directed to the cell's waste-disposal unit, the proteasome. Lindquist found that a form of the prion protein that was specifically targeted to the cytosol caused rapidly lethal neurodegeneration in mice. This protein did not acquire resistance to protein-digesting enzymes (proteases), which has long been thought to be a key characteristic of PrP^{Sc}. But proteasome inhibition led to the accumulation of a slightly protease-resistant prion protein in cultured cells. Lindquist speculated that the diverse mutations in the prion protein that are associated with familial Creutzfeldt–Jakob disease (CJD) — a human TSE — might all lead to enhanced retrotranslocation, which, upon impaired proteasome function, could trigger disease. The big surprise here is that the cytosol might be the place where PrP-mediated neuronal death begins.

However, this model was contested by D. Harris (Washington Univ., St Louis, Missouri), who found that cytosolic prion protein retains its 'signal peptide' — normally removed after proteins enter the ER — and does not contain the glycosyl phosphatidylinositol 'anchor' needed for attachment to membranes[3]. This suggests that the protein never entered the ER, and so could not have undergone retrotranslocation. Harris also pointed out that proteasome inhibitors have powerful effects on the levels of prion messenger RNA; these effects might have contributed to previous results.

Even within a single population of inbred animals, prions come in distinct varieties, which — upon transmission to further

**Keystone Symposium on Molecular Aspects of Transmissible Spongiform Encephalopathies (Prion Diseases)*. Breckenridge, Colorado, 2–6 April 2003.

100 YEARS AGO

Further particulars of the work and position of the National Antarctic Expedition have been brought by the New Zealand mail… The chief scientific work accomplished by the expedition is summarised as follows:— (1) The discovery of an extensive land at the east extremity of the great ice barrier. (2) The discovery that MacMurdo Bay is not a "bay," but a strait, and that Mounts Erebus and Terror form part of a comparatively small island. (3) The discovery of good winter quarters in a high latitude — viz. 77° 50′ S., 166° 42′ E. — with land close by suitable for the erection of the magnetic observatories, &c. The lowest temperature experienced was 92° of frost Fahrenheit. (4) An immense amount of scientific work over twelve months in winter quarters, principally physical and biological. (5) Numerous and extensive sledge journeys in the spring and summer, covering a good many thousand miles, of which the principal is Captain Scott's journey, upon which a latitude of 82° 17′ south was attained, and an immense tract of new land discovered and charted as far as 83° 30′ south, with peaks and ranges of mountains as high as 14,000 feet… As the *Discovery* has not returned to Lyttelton, there is little doubt that the expedition has been forced to spend a third winter in the Antarctic.

From *Nature* 7 May 1903.

50 YEARS AGO

In June 1952 the crew of a fisheries patrol boat cruising in Miramichi Bay, New Brunswick, observed what they took for a sand-bar in an unexpected situation. On closer inspection they found that there was no such bar, but that the surface of the sea over a wide area was in a state of violent turmoil ("a sort of boiling") due to the presence of enormous numbers of polychaetes. The area covered was some 150 yards in radius and was broken up into several minor patches… The polychaetes involved were the heteronereid forms (both sexes) of *Nereis succinea* (Leuckart). This is the first record of that species from eastern Canadian waters, though it is known from the eastern coast of the United States, usually under the name *Nereis limbata* Ehlers… We know of no other case of the swarming of a nereid with such activity and in such concentrated masses as occurred in this instance.

From *Nature* 9 May 1953.